> approach is compatible for fixing microspheres for pH indication that carry FITC functionality. The resulting array of fixed microspheres retains its pH sensitivity due to the permeability of the sulfonated Nafion to hydrogen ions. This approach, however, can not be employed generically as Nafion is impermeable to most water soluble species. A similar approach can be employed with different polymers. For example, solutions of polyethylene glycol, polyacrylamide, or polyhydroxymethyl methacrylate (polyHEMA) can be used in place of Nafion, providing the requisite permeability to aqueous species.
>
> In some embodiments it may be preferable to effect a more permanent attachment after the initial localization, for example through the use of cross-linking agents, a film or membrane over the array.

Thus, Walt et al. discuss *a sequence of* placing microspheres in fiber wells, and then use of a polymer to hold the microspheres in place. In contrast, in the present method, the encoded beads and the polymerizable components are all placed on a substrate and polymerized together, in one step. Such a process is not suggested in Walt et al., where the polymer is used to hold in place the microspheres in the wells, and the steps of placing the spheres in the well, then forming a gel, must be sequential.

Moreover, the substrate envisioned by Walt is: "any material that can be modified to contain discrete individual sites appropriate for the attachment or association of beads"[see col 5, para 3]. In the claimed invention, however, a bead assembly is formed on a planar surface, and there are no discrete sites on such a substrate. In fact, according to claim 96, the final gel embedded array is a self-supporting film and is not attached to any substrate.

The Examiner has also rejected claim 90 under Section 103(a) over Walt et al. in view of Schulz et al., alleging that Schulz et al. teach that long chain alkyl acrylamide enhance the viscosification efficiency of the co-polymers they are in. Applicants agree with the Examiner's characterization of the disclosure in Schulz et al. but note that enhancing viscosification is a teaching away from the claimed invention, as increased viscosification would further inhibit the entry of macromolecules into the gel, where they could access the bead-bound biomolecules and generate a detectable signal.

The Examiner has also rejected claims 87-88 under Section 103(a) over Walt et al. in view of Bryan et al., alleging that Bryan et al. teach use of silicon chips, adaptable for detection and identification of biological agents in a sample with a device for

integrating the output data signals and accumulating them, and generating an output device signal. The device of Bryan et al. is described in claim 1of the patent as follows:

> A microelectronic device, comprising:
>
> a substrate;
>
> a plurality of micro-locations defined on the substrate, wherein each micro-location is for linking a macromolecule;
>
> an independent photodetector integrated at each micro-location and optically coupled to each micro-location, each photodetector being configured to generate a sensed signal responsive to the photons of light emitted at the corresponding micro-location when a light-emitting chemical reaction occurs at that micro-location, each photodetector being independent from the photodetectors optically coupled to the other micro-locations; and
>
> an electronic circuit coupled to each photodetector and configured to read the sensed signal generated by each photodetector and to generate output data signals therefrom that are indicative of the light emitted at each micro-location by the light-emitting chemical reactions, whereby the device detects photons of light emitted by light-emitting chemical reactions, wherein
>
> each micro-location is defined by a portion of the surface of the device.

It is not understood how a gel as in Walt et al. could be used with the device in Bryan et al., as the gel coating on the substrate/silicon chip of Bryan et al. would overlay would create bridges among the micro-locations, preventing separate signal detection. Accordingly, the claimed invention is not suggested by Walt et al. in combination with Bryan et al.

In conclusion, all rejections have been overcome, and allowance of the application is respectfully sought.

Respectfully submitted,

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